UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/637,780	08/11/2000	Nickolai Alexandrov	2750-1096P	7984

2292 7590 01/29/2003

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
SHEINBERG, MONIKA B

ART UNIT	PAPER NUMBER
1634	10

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/637,780	ALEXANDROV ET AL.	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *25-29 and 38-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 30-37* is/are rejected.

7)☒ Claim(s) *1-3 and 5* is/are objected to.

8)☒ Claim(s) *1-50* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Election

Applicants' election of Group I (claims 1-24 and 30-37), and elected the sequence SEQ ID NO: 1; in Paper No. 9, filed 15 November 2002, is acknowledged. The claims should be amended to reflect the elected sequence. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)). Claims 25-29 and 38-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed only to nucleic acid molecules and the peptide they encode, whereas in contrast the elected claims also include constructs and recombinant host cells.

Claim Rejections - 35 USC § 112 and 101

The following is a quotation of the ***first*** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-24 and 30-37 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well-established utility.

The claimed nucleic acids of claims 1-9 are not supported by a specific asserted utility because the disclosed uses of these compositions are not specific and are generally applicable to any nucleic acid. The specification states that the nucleic acid compounds may be useful as markers, the isolation of polypeptides, hybridization probes, primers, the isolation of full-length cDNAs or genes, which would be used to make protein and optionally further usage for mapping and numerous other generic genetic engineering usages, as well as genetic therapy, such as antisense usage. In fact, the specification summarized modern biotechnology generally but never connects any of the specifically elected sequences to any particular or specific utility. This wishlist desire for a utility for the claimed sequences falls short of a readily available utility. Similarly, protein may be used for detection of expression, antibody production, Western blots, etc. These are non-specific uses that are applicable to nucleic acid(s) and/or proteins in general and not particular or specific to the nucleic acids being claimed. Claims 10-24 and 30-37 depend from 1-9 and thus also lack utility.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

Claims 1-24 and 30-37 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility, or, alternatively, a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claims 1-24 and 30-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-24 and 30-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a sequence exhibiting 100% identity to the sequences claimed in claims 1-3 and 5; does not reasonably provide enablement for any percent identity less than 100%. [Please note however this rejection is in regards specifically to the issue of claiming sequences that are not identical to the one disclosed. Overall however, as stated above, even the 100% sequence identity is not enabled.] The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to reproduce the invention commensurate in scope with these claims. The transcription, translation, folding, etc. all become effected by variance in the sequence. Any sequence obtained that is less than 100% identical is unpredictable as to retaining the some or any of the bioactivity once it deviates from 100% similarity. Therefore due to the unpredictability of the sequence results, any decrease in percent similarity to the claimed sequence is not enabled by the specification. The reverse of the claimed isolated nucleotide sequence of claim 4 would no longer carry sequence homology SEQ ID NO: 1, but would result in a completely different product of transcription results with such a change in sequence. The reading frame changes and the resulting amino acids would not create the same protein as the original nucleotide sequence. The reverse sequence lacks predictability in the amino acid sequence it encodes and the bioactivity of the resulting protein.

In addition, absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support an assertion that the biological activity of the claimed subject matter would be the same as that of a similar sequence of less than 100% homology. Note that it would have been will known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure and function although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function

following a significant amount of further research. See Attwood (*Science*, v. 290, pp. 471-473, 2000); Gerhold et al. (*BioEssays*, v.18, n.12, pp. 973-981, 1996); Wells et al. (*J. Leukocyte Biol.*, v.61, n.5, pp. 545-550, 1997); and Russel et al. (*J. Mol. Biol.*, v.244, pp. 332-350, 1994). However, this level of factual evidence is absent here.

The reverse of the claimed isolated nucleotide sequence of claim 4 lacks enablement in the manner that a completely different product of transcription results with such a change in sequence. The reading frame changes and the resulting amino acids would not create the same protein as the original nucleotide sequence. The reverse sequence lacks predictability in the amino acid sequence it encodes and the bioactivity of the resulting protein.

Claims 1-4, 6-24 and 30-37 are directed to encompass DNA gene sequences, and fragments of sequences of the provided sequences, corresponding sequences from other species, mutated fragment sequences, allelic variants, splice variants, and so forth. None of these additional sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. This is a rejection based on a lack of WRITTEN DESCRIPTION.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1; the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 1, but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Further, the following claims recite limitations to SEQ ID NO: 1 which are not present within the disclosed SEQ ID NO: 1.

Claim 6 requires that some portion and/or the entirety of SEQ ID NO: 1 comprises an open reading frame. There is no indication that some portion and/or the entirety of SEQ ID NO: 1 comprises an open reading frame in the sequence listing.

Claim 7 requires that some portion and/or the entirety of SEQ ID NO: 1 is capable of functioning as a promoter, a 3' termination sequence, an untranslated region (UTR), or as a regulatory sequence. No function and region has been identified within SEQ ID NO: 1 to be a promoter and none is apparent. Claims 14-16, 22-24, 36 and 37 entail vectors and host cells having SEQ ID NO: 1 with the recited functional limitations of claim 7 through dependency.

Claim 8 (dependent from claim 7) requires some portion and/or the entirety of SEQ ID NO: 1 to be a promoter comprising a sequence selected from the group consisting of a TATA box sequence, a CAAT box sequence, a motif of GCAATCG or any transcription-factor binding sequence, and any combination thereof. Again, no function and region has been identified within SEQ ID NO: 1 to be a promoter and none is apparent.

Claim 9 (dependent from claim 7) requires some portion and/or the entirety of SEQ ID NO: 1 to be a regulatory sequence which is capable of promoting seed-specific expression, embryo-specific expression, ovule-specific expression, tapetum-specific expression or root-specific expression of a sequence or any combination thereof. Again, no function and region has been identified within SEQ ID NO: 1 to be a promoter/regulatory sequence and none is apparent.

The following is a quotation of the ***second*** paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 and 30-37 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 and 5 are vague and indefinite as to what is meant therein by the limitation "a complement" or "complementary". A possible interpretation is that the complement must be of the same length and be the full and exact complement of the recited SEQ ID NO: 1. Another

interpretation is that any complement is meant including those with less than 100% complementarity, such as 90%, 50%, or even 10%. Clarification of the metes and bounds of the claim is requested via clearer claim wording. In addition, the independent claims 1-3 are interpreted to comprise fragments of a complement, and not only full complements. Thus this encompasses even a single nucleotide since a fragment of a complement remains inclusive of a sequence of shorter length with each base pair matched with the base pairs of the elected sequence. Claims 4, 6-24 and 30-37 are rendered vague and indefinite due to their dependency from claims 1-3.

Claim 5 is vague and indefinite as to what is meant by the limitation "a temperature from about 40° and 48°C below". A possible interpretation is that the temperature must be about 40°C and about 48°C simultaneously, which is not possible. Clarification of the metes and bounds of the claim is requested; whether the temperature is 40°-48°C or is it 40°C and 48°C at specific points time frames, etc.

Claims 6-9 are vague and indefinite with regard to the lack of structural limitation(s). Unrepresented/disclosed within the claims and specification (particularly the sequence listing) are denoted structural limitations (i.e. nucleic acid position of promoter as in instant claim 7). Should applicants believe otherwise, particular support (i.e. page and line number) for the structural limitations of SEQ ID NO: 1 is required. Claims 14-16, 22-24, 36 and 37 are rendered vague and indefinite due to their dependency from claims 6.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. § 102(b) as being anticipated by products O3378 and O8379 of the 1990 Sigma Chemical Catalog.

In The 1990 Sigma Chemical Catalog product O3378 is a 7-mer oligonucleotide of poly dT nucleotides and product O8379 is a 14-mer oligonucleotide of poly dT nucleotides. It is noted that these oligonucleotides are fragments in length as required for instant claims 1-3, and/or are at least about 86% identical to poly T segments or their complementary respective poly A segments of the instantly claimed nucleic acids. They thus anticipate instant claims 1-3 via segments therein which are poly T segments present in the SEQ ID NO: 1 (nucleic acid positions 1313-1319 and 1306-1313 respectively).

Claim Objections

Claims 1-3 and 5 are objected to for referencing a Table within the claims (M.P.E.P. § 2173.05 (s)).

Conclusion

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 1 P.M to 8 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

JEHANNE SOUAYA
PATENT EXAMINER

1/27/03

January 27, 2003

Monika B. Sheinberg
Art Unit 1634

MBS